CLAIMS

1. A compound which is a crystalline Form III of S-repaglinide.

2. The compound of claim 1, having an X-ray diffraction pattern, expressed in terms of 2 theta angles, that includes five or more peaks selected from the group consisting of 4.44 ± 0.09, 6.81 ± 0.09, 7.80 ± 0.09, 9.28 ± 0.09, 11.09 ± 0.09, 11.89 ± 0.09, 12.92 ± 0.09, 13.46 ± 0.09, 14.34 ± 0.09, 15.77 ± 0.09, 16.24 ± 0.09, 17.08 ± 0.09, 18.06 ± 0.09, 18.75 ± 0.09, 19.25 ± 0.09, 19.59 ± 0.09, 19.99 ± 0.09, 20.34 ± 0.09, 21.18 ± 0.09, 21.96 ± 0.09, 22.18 ± 0.09, 22.58 ± 0.09, 23.24 ± 0.09, 23.77 ± 0.09, 24.08 ± 0.09, 25.02 ± 0.09, 25.31 ± 0.09, 25.78 ± 0.09, 26.67 ± 0.09, 27.39 ± 0.09, 28.03 ± 0.09, 30.26 ± 0.09, 35.50 ± 0.09, and 38.74 ± 0.09 degrees.

3. The compound of claim 1, having substantially the same X-ray diffraction pattern as shown in Figure 1.

4. The compound of claim 1, having a differential scanning calorimetry thermogram which exhibits a significant endotherm peak at about 80°C.

5. The compound of claim 4, having substantially the same differential scanning calorimetry thermogram as shown in Figure 2.

6. The compound of claim 1, having an infrared absorption spectrum with absorption bands at about 3291 cm^{-1}, about 3029 cm^{-1}, about 2935 cm^{-1}, about 2795 cm^{-1}, about 1292 cm^{-1}, about 1727 cm^{-1}, about 1643 cm^{-1}, about 1611 cm^{-1}, about 1537 cm^{-1}, about 1436 cm^{-1}, about 1225 cm^{-1}, about 1171 cm^{-1}, about 1087 cm^{-1}, about 1028 cm^{-1}, about 986 cm^{-1}, about 922 cm^{-1}, about 860 cm^{-1}, about 764 cm^{-1}, about 686 cm^{-1}, and about 533 cm^{-1}.

7. The compound of claim 6, having substantially the same infrared spectrum as that shown in Figure 3.

8. A composition comprising S-repaglinide as a solid, wherein at least 80% by weight of said solid S-repaglinide is its crystalline Form III having an X-ray diffraction pattern, expressed in terms of 2 theta angles, that includes five or more peaks selected from the group consisting of 4.44 ± 0.09, 6.81 ± 0.09, 7.80 ± 0.09, 9.28 ± 0.09, 11.09 ± 0.09, 11.89 ± 0.09, 12.92 ± 0.09, 13.46 ± 0.09, 14.34 ± 0.09, 15.77 ± 0.09, 16.24 ± 0.09, 17.08 ± 0.09, 18.06 ± 0.09, 18.75 ± 0.09, 19.25 ± 0.09, 19.59 ± 0.09, 19.99 ± 0.09, 20.34 ± 0.09, 21.18 ± 0.09, 21.96 ± 0.09, 22.18 ± 0.09, 22.58 ± 0.09, 23.24 ± 0.09, 23.77

± 0.09, 24.08 ± 0.09, 25.02 ± 0.09, 25.31 ± 0.09, 25.78 ± 0.09, 26.67 ± 0.09, 27.39 ± 0.09, 28.03 ± 0.09, 30.26 ± 0.09, 35.50 ± 0.09, and 38.74 ± 0.09 degrees.

9. The composition of claim 8, wherein at least 90% by weight of said solid S-repaglinide is the crystalline Form III.

10. The composition of claim 8, wherein at least 95% by weight of said solid S-repaglinide is the crystalline Form III.

11. The composition of claim 8, wherein at least 99% by weight of said solid S-repaglinide is the crystalline Form III.

12. The composition of claim 8, wherein said solid S-repaglinide is substantially free of its crystalline Forms I and II.

13. The composition of claim 8, wherein at least 1% of said solid S-repaglinide is not the crystalline Form III.

14. The composition of claim 8, wherein at least 5% of said solid S-repaglinide is not the crystalline Form III.

15. A pharmaceutical composition comprising a) the compound of claim 1, and b) a pharmaceutically acceptable carrier or diluent.

16. The pharmaceutical composition of claim 15, further comprising one or more pharmaceutically acceptable excipients.

17. The pharmaceutical composition of claim 16, which is a solid dosage form for oral administration.

18. The pharmaceutical composition of claim 17, wherein said solid dosage form is a tablet.

19. A process for preparation of a crystalline Form III of S-repaglinide, said process comprising:

a. providing a solution of S-repaglinide in a haloalkane solvent;

b. contacting said solution with C_5-C_{10} aliphatic or alicyclic hydrocarbon anti-solvent thereby forming a precipitate; and

c. isolating the precipitate, which is the crystalline Form III of S-repaglinide.

20. The process of claim 19, further comprising drying the isolated precipitate.

21. The process of claim 19, wherein the providing step includes mixing a powder of the starting S-repaglinide with the haloalkane solvent to form said solution.

22. The process of claim 21, wherein said powder of the starting S-repaglinide is a solid form of S-repaglinide selected from the group consisting of crystalline Form I, crystalline Form II and amorphous S-repaglinide.

23. The process of claim 19, wherein the haloalkane solvent is selected from the group consisting of dichloromethane, chloroform, and dichloroethane.

24. The process of claim 19, wherein the C_5-C_{10} aliphatic or alicyclic hydrocarbon is a C_5-C_7 aliphatic or alicyclic hydrocarbon.

25. The process of claim 19, wherein the C_5-C_{10} aliphatic or alicyclic hydrocarbon is selected from the group consisting of petroleum ether, hexane, n-heptane, cyclohexane, and cycloheptane.

26. The process of claim 19, wherein the concentration of said solution is from about 0.25 gram to about 1 gram per milliliter of the haloalkane solvent.

27. The process of claim 26, wherein the concentration of said solution is from about 0.4 gram to about 0.6 gram of S-repaglinide per milliliter of the haloalkane.

28. The process of claim 27, wherein the concentration of said solution is about 0.5 gram of S-repaglinide per milliliter of the haloalkane.

29. The process of claim 19, wherein the ratio of said haloalkane to said C_5-C_{10} aliphatic or alicyclic hydrocarbon, measured volume-to-volume, ranges from about 1:1 to about 1:5.

30. The process of claim 19, wherein said ratio of said haloalkane to said C_5-C_{10} aliphatic or alicyclic hydrocarbon is about 1:3.

31. The process of claim 19, wherein the contacting step includes adding said C_5-C_{10} aliphatic or alicyclic hydrocarbon to said solution.

32. The process of claim 19, wherein said C_5-C_{10} aliphatic or alicyclic hydrocarbon is petroleum ether.

33. The process of claim 32, wherein said haloalkane is dichloromethane.

34. A compound which is the crystalline Form III of S-repaglinide produced by the process of claim 19.

35. A compound which is the crystalline Form III of S-repaglinide produced by the process of claim 33.

36. A process for preparation of a crystalline Form III of S-repaglinide, said process comprising:

a) dissolving S-repaglinide in dichloromethane;

b) adding petroleum ether to the solution to form a precipitate; and

c) isolating the precipitate, which is the crystalline Form III of S-repaglinide.

37. The process of claim 36, wherein the concentration of the dichloromethane solution is from about 0.4 to about 0.6 gram of S-repaglinide per milliliter of dichloromethane, and the ratio of dichloromethane to petroleum ether, measured volume-to-volume, ranges from about 1:1 to about 1:5.

38. A compound which an amorphous form of S-repaglinide.

39. The compound of claim 1 having substantially the same X-ray diffraction pattern as shown in Figure 4.

40. A process for making an amorphous form of S-repaglinide, said process comprising:

a) providing S-repaglinide as a solution in a lower alcohol;

b) cooling said solution so that a solid mass separates;

c) isolating said separated solid mass, which is the amorphous form of S-repaglinide.

41. The process of claim 40, further comprising drying said isolated solid mass.

42. The process of claim 40, wherein said providing step includes mixing a powder of the starting S-repaglinide and the lower alcohol, and heating the mixture to a temperature of from about 35°C to about 70°C until the solution is formed.

43. The process of claim 40, wherein the mixture is heated to from about 45°C to about 55°C.

44. The process of claim 40, wherein the solution of S-repaglinide is cooled to from about 0°C to about 5°C.

45. The process of claim 41, wherein said powder of the starting S-repaglinide is selected from the group consisting of crystalline Form I, crystalline Form II and crystalline Form III.

46. The process of claim 40, wherein the lower alcohol is selected from the group consisting of methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, and t-butanol.

47. The process of claim 40, wherein the lower alcohol is methanol.

48. A compound which the amorphous form of repaglinide produced by a process of claim 40.

49. A compound which the amorphous form of repaglinide produced by a process of claim 48.

50. A process for preparation of a crystalline Form II of S-repaglinide, said process comprising:

a) providing a solution of S-repaglinide in a solvent containing aromatic hydrocarbon with the proviso that said solvent does not include petroleum ether;

b) cooling said solution thereby a solid mass separates;

c) isolating said solid mass, which is said crystalline Form II of S-repaglinide.

51. The process of claim 50, wherein said solvent does not include any aliphatic hydrocarbon components.

52. The process of claim 50, wherein said solvent consists of said aromatic hydrocarbon.

53. The process of claim 50, wherein said aromatic hydrocarbon is selected from the group consisting of benzene, toluene, ethyl benzene and xylene.

54. The process of claim 50, wherein said aromatic hydrocarbon is toluene.

55. The process of claim 52, wherein said aromatic hydrocarbon is toluene.

56. The process of claim 50, wherein the providing step includes mixing a powder of the starting S-repaglinide with the solvent and heating said mixture to form the solution.

57. The process of claim 50, further comprising drying the isolated solid mass.